IN THE CLAIMS

Please delete all prior lists of claims in the application and insert the following list of claims:

1. (CANCELED) ~~A method for cloning genes of a biosynthetic pathway, comprising:~~

~~i) providing host cells containing a replicable vector including genomic DNA isolated from a source of uncultivated microrganisms, which host cells are provided under conditions wherein expression of open reading frame sequence(s) of the genomic DNA occurs; and~~

~~ii) detecting the presence or absence of a biosynthetic pathway which is dependent on expression of at least one of the opening reading frames by the host cells.~~

2. (CURRENTLY AMENDED) A method for ~~identifying~~ **detecting** a compound produced by a biosynthetic pathway, comprising**:**

i) ~~providing host cells containing a replicable vector including genomic DNA isolated from a source of uncultivated microrganisms, which host cells are provided under conditions wherein expression of open reading frame sequence(s) of the genomic DNA occurs~~ **isolating genomic DNA from a source containing uncultivated microorganisms, without an intervening step of isolating or culturing cells from the source, by mixing the source with an extraction buffer and lysing the microorganisms to obtain isolated genomic DNA**; and **then**

**ii) inserting the isolated genomic DNA of step (i) into a replicable vector to obtain clones of the replicable vector comprising the isolated genomic DNA; and then**

**iii) introducing the clones of step (ii) into host cells to obtain a library of host cells, wherein the isolated genomic DNA in at least some of the clones is at least 50 kb; and then**

**iv) culturing the host cells of step (iii) under conditions wherein an open reading frame sequence of the isolated genomic DNA is expressed by the host cells; and then**

~~ii~~ **v)** detecting **a** compound produced by the host cells **as a result of expression of the open reading frame sequence of step (iv)**.

3. (CURRENTLY AMENDED) The method of claim 2, wherein ~~the biosynthetic pathway produces or transmutes~~ **step (v) comprises detecting** a non-polymeric compound.

4. (CURRENTLY AMENDED) The method of claim 2, wherein ~~the biosynthetic pathway produces or transmutes~~ **step (v) comprises detecting** a non-proteinaceous compound.

5. (CURRENTLY AMENDED) The method of claim 2, wherein ~~the biosynthetic pathway produces~~ **step (v) comprises detecting** a compound having a molecular weight less than 7500 amu.

6. (CURRENTLY AMENDED) The method of claim 2 ~~[[ 5]]~~, wherein **step (v) comprises detecting a** ~~the~~ compound **that** is a direct product of endogenous precursors for the biosynthetic pathway.

7. (CANCEL) ~~The method of claim 2 [[ 5]], wherein the compound is synthesized de novo.~~

8. (CURRENTLY AMENDED) The method of claim 2, wherein **in step (iii)** the ~~vector includes at least 20 kilobases of~~ **isolated** genomic DNA **in the clones has an average length of at least 75 kb**.

9. (CURRENTLY AMENDED) The method of claim 8, wherein **in step (iii)** the ~~vector includes at least 50 kilobases of~~ **isolated** genomic DNA **in the clones has an average length of at least 100 kb**.

10. (CURRENTLY AMENDED) The method of claim 2, wherein the source of ~~uncultivated microorganisms~~ **microorganisms in step (i)** includes ~~prokaryotic cells~~ **prokaryotes**.

11. (CURRENTLY AMENDED) The method of claim 10, wherein the source of ~~uncultivated microorganisms~~ **microorganisms in step (i)** includes ~~prokaryotic cells~~ **prokaryotes** of the Archaea Domain.

12. (CURRENTLY AMENDED) The method of claim 11, wherein the source of ~~uncultivated microorganisms~~ **microorganisms in step (i)** includes Archaea cells selected from the group consisting **of** Crenarachaeota, Euryarachaeota, Karachaeota, and combinations thereof

13. (CURRENTLY AMENDED) The method of claim 2, wherein **step (i) comprises isolating genomic DNA from a source selected from the group consisting of** ~~the uncultivated microorganisms are isolated from~~ soil samples, insect intestines, plant rhizospheres, microbial mats, sulfur pools samples, or marine samples.

14. (CURRENTLY AMENDED) The method of claim 2, wherein the source of ~~uncultivated microorganisms~~ **microorganisms in step (i)** includes prokaryotes having low ~~low~~ G/C content genomes.

15. (CURRENTLY AMENDED) The method of claim 2, wherein the source of uncultivated ~~microorganisms~~ **microorganisms in step (i)** includes ~~anerobes~~ **anaerobes**.

16. (CURRENTLY AMENDED) The method of claim 2, wherein **in step (iii)** the **library of** host cells ~~comprise~~ **comprises** a variegated population of vectors containing different **isolated** genomic DNA sequences.

17. (CURRENTLY AMENDED) The method of claim 16, wherein **step (i) comprisies isolating** genomic DNA ~~has~~ **having** an average length of at least ~~20~~ **50** kilobases ~~in length~~.

18. (CURRENTLY AMENDED) The method of claim 16, wherein **in step (iii) the library of host cells comprises a** variegated population of vectors ~~include~~ **including isolated** genomic DNA from at least 10 different microorganism species.

19. (CURRENTLY AMENDED) The method of claim 2, wherein **step (iii) comprises introducing the clones of step (ii) into** ~~the~~ host cells ~~are a species of Bacteria~~ selected from the group consisting of Acetobacter, Actinomyces, Aerobacter, ~~Agribacterium~~ **Agrobacterium**, Azotobacter, Bacillus, Bacteroides, Bordetella, Brucella, Chlamydia, Clostridium, Corynebacterium, Erysipelothrix, Escherichia, Francisella, Fusobacterium, Haemophilus, Klebsiella, Lactobacillus, Listeria, Mycobacterium, Myxococcus, Neisseria, Nocardia, Pasteurella, Proteus, Pseudomonas, Rhizobium, Rickettsia, Salmonella, Serratia, Shigella, Spirilla, Spirillum, Staphylococcus, Streptococcus, Streptomyces, Trepanema, Vibrio, ~~Vibrio,~~ and Yersinia.

20. (CURRENTLY AMENDED) The method of claim 19, wherein **step (iii) comprises introducing the clones of step (ii) into** ~~the~~ host cells ~~are a species~~ **selected from the group consisting** of Escherichia ~~or~~ **and** Streptomyces.

21. (CURRENTLY AMENDED) The method of claim 20, wherein **step (iii) comprises introducing the clones of step (ii) into** ~~the host cells are~~ **an** *Escherichia coli* **host cell**.

22. (CURRENTLY AMENDED) The method of claim 2, wherein **step (ii) comprises inserting the isolated genomic DNA into** ~~**the vector is**~~ a low-copy number vector.

23. (CURRENTLY AMENDED) The method of claim 22, wherein **step (ii) comprises inserting the isolated genomic DNA into** ~~**the vector is**~~ a single-copy number vector.

25. (CURRENTLY AMENDED) The method of claim 2, wherein **step (v) comprises detecting** ~~**production of**~~ the compound **produced by the host cells as a result of expression of the open reading frame sequence of step (iv)** ~~**is detected**~~ by an ability **of the host cell** to ~~**induces**~~ **induce** a biological or biochemical response from a test cell.

26. (CURRENTLY AMENDED) The method of claim ~~2~~ **25**, wherein the **biological or bichemical** response ~~**from**~~ **induced in the** test cell comprises: a phenotypic change, a change in gene transcriptional rates, a change in phosphorylation states, a change in 2nd messenger formation, cell quiescence, **or** cell death.

27. (CURRENTLY AMENDED) The method of claim 2, wherein **step (v) comprises detecting** ~~**production of**~~ the compound **produced by the host cells as a result of expression of the open reading frame sequence of step (iv)** ~~**is detected**~~ by spectrometric detection.

28. (CURRENTLY AMENDED) The method of claim 2, wherein **step (v) comprises detecting** ~~**production of**~~ the compound **produced by the host cells as a result of expression of the open reading frame sequence of step (iv)** ~~**is detected**~~ by chromatographic detection.

29. (CURRENTLY AMENDED) The method of claim 2, wherein **step (v) comprises detecting** ~~**production of**~~ the compound **produced by the host cells as a**

**result of expression of the open reading frame sequence of step (iv)** ~~**is detected in**~~ **using** a cell-free assay.

30. (CURRENTLY AMENDED) The method of claim 2, wherein **step (v) comprises detecting** ~~**production of**~~ the compound **produced by the host cells as a result of expression of the open reading frame sequence of step (iv)** ~~**is detected**~~ by **inducing** ~~**an ability to induces**~~ a biological or biochemical response from the host cell.

31. (CANCELED) ~~The method of claim 1, comprising the further step of identifying or isolating individual genes from the genomic DNA which produce biosynthetic pathway.~~

32. (CANCEL) ~~The method of claim 2, comprising a further step of identifying the chemical structure of compound.~~

33. (CANCEL) ~~The method of claim 2, comprising a further step of formulating a pharmaceutical composition including one or more compounds produced by the host cell.~~

34. (CANCEL) ~~A cell engineered with a replicable vector including heterologous genomic DNA isolated from a source of uncultivated microrganisms, which host cell produces a compound in a manner dependent on expression of at least one opening reading frame of the genomic DNA.~~

35. (CANCEL) ~~A library of cells comprising a replicable vector including heterologous genomic DNA isolated from a source of uncultivated microrganisms, wherein the library includes a variegated population of genomic DNA sequences, and at least a portion of the cells produce a compound in a manner dependent on expression of at least one opening reading frame of the genomic DNA.~~

36. (CANCEL) ~~An isolated nucleic acid comprising one or more genes from a source of uncultivated microrganisms, wherein expression of the genes in a heterologous host cell provides a functional biosynthetic pathway for production of a compound in a manner dependent on expression of the genes.~~

37. (CANCEL) ~~A purified form of a compound which can be produced by the cell of claim 34.~~

38. (CANCEL) ~~A pharamaceutical preparation of a compound which can be produced by the cell of claim.~~

39. (CANCEL) ~~A library of compounds produced by the cells of claim 35.~~

40. (CANCELED) ~~A method for cloning genes of a biosynthetic pathway, comprising~~

~~i) cloning, into a replicable vector, genomic DNA isolated from a source of uncultivated microrganisms;~~

~~ii) expressing open reading frame sequence(s) of the genomic DNA in host microorganisms that harboring the vector; and~~

~~iii) detecting the presence or absence of a biosynthetic pathway which is dependent on expression of at least one of the opening reading frames by the host microorganisms.~~

41. (CURRENTLY AMENDED) A method for ~~identifying~~ **detecting** a product of a biosynthetic pathway, comprising

i) **directly** cloning~~,~~ into a replicable vector~~,~~ genomic DNA isolated from a ~~source of uncultivated microrganisms~~ **complex microbial sample without an intervening step of isolating or culturing cells from the sample, and size-fractionated prior to any enzymatic manipulation of the DNA to facilitate its insertion into the replicable vector, wherein at least some of the genomic DNA cloned into the vector is at least 50 kb long**; **and then**

**ii) transforming the replicable vector of step (i) into host cells to obtain a library of host cells; and then**

~~ii~~ **iii)** expressing open reading frame sequence(s) of the genomic DNA ~~**in host microorganisms harboring the vector**~~ **contained in the library of host cells of step (ii)**; and **then**

~~iii~~ **iv)** detecting a compound which is the product of a biosynthetic pathway that is dependent on expression of at least one of the opening reading frames **of step (iii)** ~~**by the host microorganisms**~~.

42. (CANCEL) ~~A method for identifying a small molecule produced by a microorganism, comprising~~

~~i) providing one or more host cells, a plurality of which each contain a replicable vector including genomic DNA isolated from a source of uncultivated microrganisms,~~

~~ii) maintaining the host cells under conditions permitting gene expression; and~~

~~iii) detecting the presence of a small molecule produced by one or more of the host cells transfected with the genomic DNA.~~

43. (CANCEL) ~~A method for identifying a genetically engineered host cell which produces a small molecule of interest, comprising~~

~~i) providing one or more host cells, a plurality of which each contain a replicable vector including genomic DNA isolated from a source of uncultivated microrganisms,~~

~~ii) maintaining the host cells under conditions permitting gene expression;~~

~~iii) detecting the presence of a small molecule produced by one or more of the host cells transfected with the genomic DNA; and~~

~~iv) identifying the host cell which produces the small molecule.~~

44. (CANCEL) ~~A method for producing a small molecule of interest, comprising~~

~~i) providing a host cell which contains genomic DNA originally isolated from a source of uncultivated microorganisms; and~~

~~ii) maintaining the host cell in a culture medium and under conditions permitting the production of the small molecule.~~

45. (CANCEL) ~~A method of claim [[2C]] 44 which further comprises separately recovering the small molecule from the host cells and medium.~~

46. (NEW) The method of claim 2, wherein step (i) comprises lysing the microorganisms and isolating the genomic DNA from the source by further treating the source with a protease and a detergent to yield a mixture, centrifuging the mixture to yield a supernatant, extracting the supernatant with chloroform in the absence of phenol to yield a chloroform fraction containing the genomic DNA, and precipitating the DNA by adding isopropanol to the chloroform fraction.

47 (NEW) The method of claim 46, wherein step (i) further comprises size-fractionating the isolated genomic DNA prior to enzymatic manipulation of the DNA for insertion into the replicable vector of step (ii).

48 (NEW) The method of claim 47, wherein step (i) comprises size-fractionating the isolated genomic DNA via electrophoresis.